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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/778,168	WRIGHT ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-19,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1,3-19,21 and 22* is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 2 February 2006 in which the previous rejections were traversed.

The previous rejections in the Office Action dated 2 September 2005 are withdrawn in view of new grounds for rejection. Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1, 3-19, 21-22 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 3-4, 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Meijer et al (WO 95/22626, published 24 August 1995).

Regarding Claim 1, Meijer et al disclose a method for identifying a single nucleotide polymorphism (e.g. a polymorphic site in HPV strains), the method comprising hybridizing a detector primer (oligonucleotide vi) to the target wherein the detector primer is complementary to the target and comprises a diagnostic nucleotide for the polymorphism located 2 to four nucleotides 5' of the 3' nucleotide:

> The oligonucleotide (vi) is derived from SEQ ID NO:2 or from its complementary sequence by from 1 to 5 nucleotide substitutions.

> Preferably, as in the case of oligonucleotide (ii), said substitutions concern substitutions occurring between different HPV strains. For example, the 11th nucleotide (C) is substituted in many strains by T (in HPV6B, HPV13, HPV31, HPV39, HPV42, HPV51, HPV52, HPV53 and HPV56). The 21st nucleotide (T) is substituted by A in several strains (in HPV11, HPV13, HPV31 and HPV52). The 23rd nucleotide (T) is substituted by C in several strains (in HPV6B, HPV11, HPV39 and HPV51). (page 11, lines 3-21).

Meijer et al further amplify the target by hybridization and extension in an isothermal amplification reaction (e.g. NASBA, page 9, lines 10-26 and Claim 20), determining the efficiency of primer extension to detect the presence of the polymorphism (page 14, lines 27).

Regarding Claim 3, Meijer et al disclose the method wherein multiple detector primers are used, each comprising a different diagnostic nucleotide (e.g. oligonucleotide (ii), page 7, lines 15-22 and page 12, line 33-page 13, line 5).

Regarding Claim 4, Meijer et al disclose the method wherein the two primers are used to identify which polymorphism is present (i.e. (ii) identifies HPV 32, 39, 57, 42 , 51 (page 7, lines 18-21) and (vi) identifies HPV 11, 13, 31, 52, 6B, 39 and 51 (page 11, line 9-12)).

Regarding Claim 13, Meijer et al disclose the method of amplification is NASBA (page 9, lines 10-26).

Regarding Claim 14, Meijer et al disclose the method wherein the detector primers are 12-50 nucleotides (i.e. 23-mer or 25-mer, page 5, lines 26-27 and page 11, lines 15-21).

Regarding Claim 15, Meijer et al disclose the method wherein the detector primers are 12-24 nucleotides (i.e. 23-mer, page 5, lines 26-27).

Regarding Claim 16, Meijer et al disclose the method wherein the detector primers are "about" 12-19 nucleotides i.e. 23-mer or a fragment of (v), (vi), (viii), (ix), or (x) (page 5, lines 26-27 and page 10, lines 19-20).

Regarding Claim 17, Meijer et al disclose the method wherein the presence or absence of the polymorphism is detected by means of a label (i.e. the extended primer is detected by hybridization with a labeled probe, page 15, lines 17-21 and page 17, lines 14-16).

Regarding Claim 18, Meijer et al disclose the method wherein the label becomes detectable upon extension of the primer (i.e. the extended primer is detected by hybridization with a probe, page 15, lines 17-21).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 5, 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer et al (WO 95/22626, published 24 August 1995) further in view of Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996).

Regarding Claim 5, Meijer et al disclose a method for identifying a single nucleotide polymorphism (e.g. a polymorphic site in HPV strains), the method comprising hybridizing a detector primer (oligonucleotide vi) to the target wherein the detector primer is complementary to the target and comprises a diagnostic nucleotide for the polymorphism located 2 to four nucleotides 5' of the 3' nucleotide:

> The oligonucleotide (vi) is derived from SEQ ID NO:2 or from its complementary sequence by from 1 to 5 nucleotide substitutions. Preferably, as in the case of oligonucleotide (ii), said substitutions concern substitutions occurring between different HPV strains. For example, the 11th nucleotide (C) is substituted in many strains by T (in HPV6B, HPV13, HPV31, HPV39, HPV42, HPV51, HPV52, HPV53 and HPV56). The 21st nucleotide (T) is substituted by A in several strains (in HPV11, HPV13, HPV31 and HPV52). The 23rd nucleotide (T) is substituted

by C in several strains (in HPV6B, HPV11, HPV39 and HPV51). (page 11, lines 3-21).

Meijer et al amplify the target by hybridization and extension in an isothermal amplification reaction (e.g. NASBA, page 9, lines 10-26 and Claim 20), determining the efficiency of primer extension to detect the presence of the polymorphism (page 14, lines 27).

Meijer et al further teach the method wherein the detector primers are selected from oligonucleotide (ii) and from oligonucleotide (vi) (page 13, line 30-page 14, line 4). Each group of oligonucleotides (ii) and (vi) contain multiple polymorphism-specific detector primers (page 7, lines 15-22 and page 11, lines 15-21). While Meijer et al teach multiple primers, they are silent regarding the use of four detector primers in a reaction.

However use of four detector primers was well known in the art at the time the claimed invention was made as taught by Caskey et al.

Caskey et al teach a similar a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. $\beta+$ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54) wherein 4 detector primers are used for differentiation of two alleles (Example 4). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the 4 detector primers of Caskey et al to the polymorphism detection of Meijer et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success for the benefit of discriminating between two alleles simultaneously as illustrated by Caskey et al (Example 4).

Regarding Claims 7-10, Meijer et al are silent regarding nondiagnoistic mismatches. However, Caskey et al teach the similar method wherein nondiagnostic mismatches are

positioned adjacent the diagnostic nucleotide thereby increasing the difference between the sequence of interest and other sequences so as favor the amplification of the sequence of interest (Column 5, lines 20-56). Caskey et al also teach the primers are preferably 12-16 (Column 4, lines 39-40) and they illustrate diagnostic nucleotides positioned 5 bases from the terminal nucleotide (Examples 3-4). They do not specifically teach the non-diagnostic nucleotide 5 nucleotides from or adjacent to the diagnostic nucleotide. However, the addition of a non-diagnostic nucleotide (as they clearly suggest) to their exemplified 12 nucleotide primers would position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide. Hence, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add a non-diagnostic nucleotide to the diagnostic primer of Caskey and to position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide based on the available nucleotide positions within the 12 nucleotide primers exemplified by Caskey et al.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Meijer et al by adding a nondiagnostic mismatch. One of ordinary skill in the art would have been motivate to so with a reasonable expectation of success based on the teaching of Caskey et al and for the expected benefit of favoring the amplification of the sequence of interest as taught by Caskey et al (Column 5, lines 20-56).

Regarding Claim 11, Meijer et al disclose the method wherein the detector primers are 15-36 nucleotides (i.e. 23-mer or 25-mer, page 5, lines 26-27 and page 11, lines 15-21).

Regarding Claim 12, Meijer et al disclose the method wherein the detector primers are 18-24 nucleotides (i.e. 23-mer, page 5, lines 26-27).

6. Claims 6, 18-19, 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meijer et al (WO 95/22626, published 24 August 1995) further in view of Whitcombe et al (U.S. Patent No. 6,326,145, filed 25 November 1998).

Regarding Claims 6 and 18-19, 21-22, Meijer et al disclose a method for identifying a single nucleotide polymorphism (e.g. a polymorphic site in HPV strains), the method comprising hybridizing a detector primer (oligonucleotide vi) to the target wherein the detector primer is complementary to the target and comprises a diagnostic nucleotide for the polymorphism located 2 to four nucleotides 5' of the 3' nucleotide. Meijer et al do not teach primers labeled using art recognized techniques (Column 6, lines 16-35) but they do not teach tailed primers, primers detectable upon extension, primers labeled with donor/quencher dyes, quantitatively detected and displaced by an upstream primer.

However, these elements were well known in the art at the time the claimed invention was made as taught by Whitcombe et al (Column 4, lines 31-65) wherein binding results in abolished signal (Column 4, lines 49-53). Whitcombe et al further teach their method is useful for strand displacement (Column 5, lines 57-59) and especially quantitative allele discrimination (Column 6, lines 33-43 and Column 10, line 60-Column 11, line 17).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the tailed primers having donor/quencher dye attached as taught by Whitcombe et al to the allele-specific primers of Meijer et al for the expected benefit of providing quantitative analysis of clinically important nucleic acids e.g. HIV nucleic acids as taught by Whitcombe et al (Column 6, lines 33-43).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 3-19 and 21-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 13-14, 16-17 and 19-23 of copending Application No. 10/202,896. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to method for detecting a single nucleotide difference in target nucleic acids and differ only in the arrangement of the limitations within the claim sets. For example, instant Claim 1 defines the detector primer as having a diagnostic nucleotide two to four nucleotides 5' of the 3' nucleotide while dependent claim 7 defines the '896 diagnostic nucleotide as N-1 to N-4. As such the claim sets are drawn to methods that are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

9. Applicant has not provided any arguments traversing the above rejection. Therefore, the rejection is maintained and made FINAL>

10. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
April 13, 2006